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Signed this 2nd day of February, 2006

A handwritten signature in black ink, consisting of several loops and a long horizontal stroke at the end.

Kumiko Kawai

Patent Department



[Name of Document]            Specification

[Title of Invention]        AUTOMATIC SAMPLER

[Claims]

[Claim 1] An automatic sampler comprising:

    a plurality of sample vessels;

    a needle made of metal for collecting liquid samples sequentially from sample vessels, with a surface of said needle being coated with a coating material, said coating material being lower in chemical activity than base metal of said needle.

[Claim 2] An automatic sampler according to Claim 1, wherein noble metal plated or deposited on said base metal of said needle is used as said coating material.

[Claim 3] An automatic sampler according to Claim 1, wherein a synthetic resin coating is used as said coating material.

[Claim 4] An automatic sampler according to Claim 1, wherein a quartz thin film formed on said base metal of said needle by a chemical vapor deposition method is used as said coating material. [Detailed Description of the Invention]

[0001]

[Technical Field to which the Invention Belongs]

    The present invention relates to an automatic sampler for an analyzing apparatus aiming at performing liquid analysis, such as a liquid chromatograph, and particularly relates to an improvement of a needle for sampling.

[0002]

[Prior Art]

Fig. 4 shows, by way of example, a main portion of flow path arrangement of an automatic sampler for a liquid chromatograph.

In Fig. 4, a plunger 3 is designed to perform a reciprocating motion by mechanical force. Sample liquid to be analyzed is enclosed in a large number of vials (small-volume sample bottles) 8 in advance, and the vials 8 are arrayed on a rack 81. A needle 7 which collects samples from the vials 8 is connected to an injector valve 1 through a looped flexible pipe (hereinafter referred to as "loop") 6. In addition, the needle 7 is retained by a not-shown drive mechanism so that the needle 7 can move freely among the vials 8, a rinse port 9 and an injection port 5 in accordance with a program. A valve 2 is a six-position rotary valve for switching a flow path of liquid sucked and discharged by the plunger 3. The reference numeral 4 represents a rinse bottle.

The injector valve 1 is connected to a liquid chromatograph apparatus 10 through pipes so as to introduce sample liquid into a flow of mobile phase liquid in the liquid chromatograph apparatus 10.

[0003]

An example of an operation sequence of sample injection using an analyzing auto-injector configured thus will be described below.

(1) When the valve 2 is located in a position to communicate with a port 0-b as shown in Fig. 4, the needle 7 is inserted into a vial 8, and the plunger 3 is pulled to suck a predetermined quantity of sample liquid. The sucked sample liquid stays in the loop 6 so as not to reach the valve 2 or the plunger 3.

(2) The needle 7 is pulled out from the vial 8 and moved to the injection port 5.

(3) The injector valve 1 is operated to introduce the sample in the loop 6 into the flow path of the mobile phase liquid. Thus, analysis of the liquid chromatograph is started.

(4) After the needle 7 is moved to a vial 8 having a sample to be analyzed next, the operations (1) to (3) are repeated.

[0004]

As described above, a step of rinsing the needle 7 is necessarily included in the automatic sampler after any sample is sampled. This step is very important to avoid mixing a preceding sample into a sample to be sampled this time (cross contamination).

In the related art, measures chiefly against physical contamination have been taken to prevent cross contamination produced through the intermediation of the needle 7. For example, rinsing was enhanced, or the surface of the needle 7 was polished and smoothed to prevent dirt from adhering thereto. However, contamination of the needle 7 is not limited to such physical one.

[0005]

[Problems that the Invention is to Solve]

Stainless steel is used as the material of the needle 7. Stainless steel is an alloy with an iron base. Therefore, iron is exposed on the surface of stainless steel microscopically, and some kind of sample component is adsorbed on the iron portion due to the chemical properties of iron. For example, a chemically adsorptive phenomenon is easily produced in basic matter because its hydroxyl group is attracted to iron in the surface of stainless steel. The sample component once adsorbed chemically cannot be removed easily even if it is rinsed physically with organic-solvent-based detergent. Such a sample component adsorbed on the surface of the needle 7 and remaining after rinsing is partially mixed into a sample to be analyzed next when the sample is sampled. Thus, cross contamination is, though slightly, brought about.

Such slight cross contamination caused by chemical adsorption has been heretofore overlooked substantially.

[0006]

In recent years, however, with advances in analytic sensitization, it has come required to take effective measures against such slight cross contamination.

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The invention was developed in consideration of such circumstances. It is an object of the invention to provide

an automatic sampler in which contamination caused by chemical adsorption and still remaining after measures against physical contamination are taken on the surface of a needle is restrained so that the automatic sampler can perform highly sensitive analysis.

[0007]

[Means for Solving the Problems]

In order to attain the foregoing object, according to the invention, surface treatment for reducing particularly chemical adsorption is given to a needle in an automatic sampler.

That is, the surface of a needle made of metal is coated with a coating material which is lower in chemical activity than base metal of the needle. More specifically, the surface of the needle is plated with noble metal such as gold or platinum. Alternatively, the surface of the needle is coated with synthetic resin such as PEEK superior in chemical resistance. It is possible to obtain a practically sufficient antifouling effect even against contamination coming from chemical adsorption which contamination cannot be removed sufficiently only by related-art measures against physical contamination. Thus, it is possible to provide an automatic sampler which can perform highly sensitive analysis.

[0008]

[Mode for Carrying Out the Invention]

Figs. 1A and 1B show needles 7 according to embodiments

of the invention.

The needle 7 shown in Fig. 1A is a flat-head needle having an outer diameter of 1.2 mm and an inner diameter of 0.5 mm and having a flat head having a flat end and a diameter is 0.65 mm. Base metal B is made of stainless steel, and the surface of the base metal B is coated with a platinum-plated layer T having a thickness of several  $\mu\text{m}$ . The surface of this needle is covered with the platinum-plated layer T which is much lower in adsorptive activity than stainless steel. Therefore, when the needle 7 is used for the automatic sampler shown in Fig. 4, chemical adsorption on the surface of the needle 7 is restrained so that the effect to reduce cross contamination is enhanced.

[0009]

In the needle 7 shown in Fig. 1B, base metal B is coated with a synthetic resin coating P (about 300  $\mu\text{m}$  thick) in place of metal plating. The synthetic resin coating P is made of PEEK (polyetheretherketone) which is a synthetic resin superior in chemical resistance and mechanical strength. As the coating method, a powder coating method can be applied. Not to say, in this case, the dimensions of the base metal B have to be made somewhat slender in advance in consideration of the thickness of the synthetic resin coating P.

PEEK is an organic material. Therefore, PEEK hardly shows a chemical adsorptive property. In addition, as is understood from the fact that PEEK is used as a material for piping in a

liquid chromatograph, PEEK shows superior resistance to various chemicals used in a liquid chromatograph. Thus, PEEK can be preferably used for the needle 7 in the automatic sampler for a liquid chromatograph.

[0010]

Figs. 2A and 2B and Figs. 3A and 3B are graphs of experimental data showing the cross contamination reduction effect when the needle 7 coated with the platinum-plated layer T was used.

In these experiments, a solution in which strong basic chlorhexidine hydrochloride was diluted with liquid the same as mobile phase liquid was sampled. An area A of a peak obtained thus was calculated. Subsequently, only the mobile phase liquid (blank sample) was analyzed so that an area B of a peak appearing for the same retention time was measured. The degree of cross contamination was expressed by a ratio C (%) of B to A.

[0011]

Figs. 2A and 2B show the case where a related-art needle made of stainless steel alone was used. Fig. 2A shows the result of analysis of the chlorhexidine hydrochloride solution, and Fig. 2B shows the result of analysis of the blank sample carried out following the analysis in Fig. 2A. From respective area values, cross contamination C is calculated by:

$$C = 9340 / 39637446 = 0.024\%$$

Next, Figs. 3A and 3B show the results of analysis in the case where the needle 7 coated with the platinum-plated layer



T was used. Cross contamination C in this case is calculated by:

$$C=321/49126387=0.00065\%$$

From these results, it is understood that the degree of cross contamination is reduced to about 1/40 when the needle 7 is coated with the platinum-plated layer T, and a remarkable improvement effect can be obtained.

[0012]

Incidentally, the setting conditions of the liquid chromatograph in these experiments are as follows.

mobile phase: 100 mM perchloric acid containing  
phosphoric acid buffer (pH 2.6) : acetonitrile = 45:55

flow rate: 0.2 mL/min

column: VP-ODS  $\phi$ 2mm $\times$ 150mm

oven temperature: 40°C

detector: UV 260 nm

sample: chlorhexidine hydrochloride 12 mg/10 mL

mobile phase

injection rate: 2  $\mu$ L

[0013]

According to the invention, the surface of the needle 7 is covered with a coating material lower in activity than the base metal B of the needle 7. The coating material is not limited to the examples. For example, also when the base metal B is plated with noble metal such as any other element of the platinum

group or gold in place of platinum, it is possible to obtain an effect equal to or close to that in the case of platinum. In addition, when the base metal B is plated with non-noble metal such as nickel or chromium lower in chemical activity than iron, a deserved improvement effect can be expected though it comes short of that in the case where the base metal B is plated with noble metal.

On the other hand, it can be considered that PFE (polyfluorethylene), or PE (polyethylene) is used in place of PEEK for coating with the synthetic resin coating P. In this case, an effect corresponding to the properties of such a raw material can be expected.

[0014]

In the embodiment, only the outer surface of the needle 7 is covered with a coating material, but the inner surface of the needle 7 is not coated. Therefore, there is a fear that the surface of stainless steel having high adsorptive activity is exposed on the inner surface and remains as a cause of cross contamination. However, the surface area of the inner surface is smaller than 20% of the total surface area of the needle 7, and hence the influence of the inner surface is not very significant. In addition, the inner surface of the needle 7 can be rinsed efficiently if the pressure and flow rate of rinse are increased. Thus, the influence of the metal surface of the inner surface on contamination is limited to an ignorable extent.

[0015]

However, to require a greater cross contamination reduction effect, it is desired that the inner surface of the needle 7 is also coated with an inactive material.

With a chemical vapor deposition method (CVD) already known as a method for coating the inner surface of a capillary, a metal thin film can be formed also on the inner surface of the needle 7. In addition, the inactive material is not limited to metal, but a thin film of high-purity quartz may be formed. Coating an inner wall of a capillary with a quartz thin film is a method put into practical use for treating the inner surface of a column in a gas chromatograph. High-purity quartz is extremely low in adsorptive activity so that contamination can be reduced to the utmost by this treatment.

[0016]

The needle 7 according to the invention can be applied to any automatic sampler of such a type that liquid samples are sampled sequentially from a plurality of vials 8 through the needle 7, including the automatic sampler having a main portion of a flow path shown in Fig. 4. In addition, the needle 7 may be applied broadly to not only automatic samplers for liquid chromatographs but also automatic samplers for various analyzing apparatuses aiming at performing liquid analysis.

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Incidentally, numerical values of dimensions shown in Figs. 1A and 1B are shown by way of example. The invention is not

limited to such values. In addition, the material of the base metal B of the needle 7 is not limited to stainless steel.

[0017]

[Effects of the Invention]

As described above in detail, the invention pays attention to the fact that contamination still remaining after a needle is rinsed is caused by chemical adsorption in a related-art automatic sampler. In order to solve the problem, the invention uses a coating material low in chemically adsorptive activity to be applied to the surface of the needle. When the automatic sampler according to the invention is combined with a liquid chromatograph, disturbance due to cross contamination is eliminated so that analysis can be made highly sensitive.

[Brief Description of the Drawings]

[Fig. 1]

Fig. 1 is a diagram showing embodiments of the invention;

[Fig. 2] Fig. 2 is a graph of experimental data showing the results of the invention;

[Fig. 3] Fig. 3 is a graph of experimental data showing the results of the invention; and

[Fig. 4] Fig. 4 is a diagram showing an example of a main portion of a flow path of an automatic sampler for a liquid chromatograph.

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[Description of the Reference Numerals and Signs]

B ...base material

T ...platinum-plated layer

P ...synthetic resin coating

7 ... needle

[Designation of Document] Abstract

[Abstract]

[Problem] Cross contamination caused by the intermediation of a needle is reduced in an automatic sampler for liquid analysis.

[Means for Resolution] The surface of a needle made of metal for collecting samples is coated with a coating material lower in chemical activity than base metal of the needle. More specifically, the surface of the needle is coated with a platinum-plated layer of gold or platinum. Alternatively, the surface of the needle is coated with a synthetic resin coating of PEEK superior in chemical resistance. As a result, it is possible to obtain a practically sufficient antifouling effect even on contamination coming from chemical adsorption. Such contamination could not be removed sufficiently only by related-art measures against physical contamination. Thus, it is possible to provide an automatic sampler which can perform highly sensitive analysis.

[Selected Drawing] Fig. 1

Drawing

[Fig. 1]

(a)

B Base Metal

T Platinum Plated Layer

7 Needle

(b)

B Base Metal

P Synthetic Resin Coating

7 Needle

[Fig. 2A]

a Injection

b Detector

c Peak No.

d Retention Time

e Area

f Height

(b)

a Injection

b Detector

c Peak No.

d Retention Time

e Area

f Height

[Fig. 3]

(a)

a Injection

b Detector

c Retention Time

d Area

e Height

(b)

a Injection

b Detector

c Retention Time

d Area

e Height

[Fig. 4]

1 Injector Valve

2 Valve

3 Plunger

4 Cleansing Liquid Bottle

5 Injection Port

6 Loop

7 Needle

8 Vial

9 Cleansing Port

10 Liquid Chromatograph Apparatus

81 Rack

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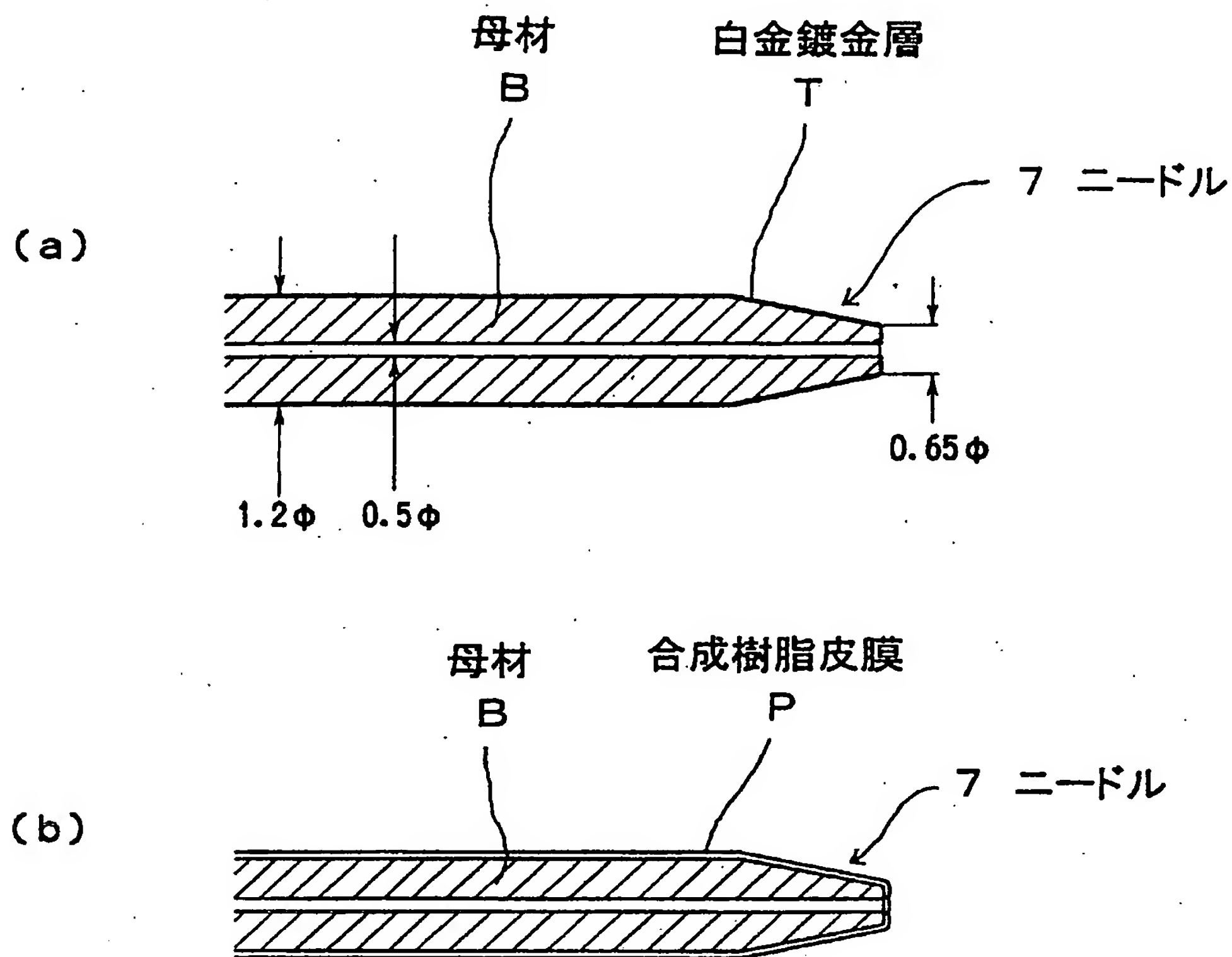
a Liquid Feed Unit

b Column



【書類名】 図面 Drawing

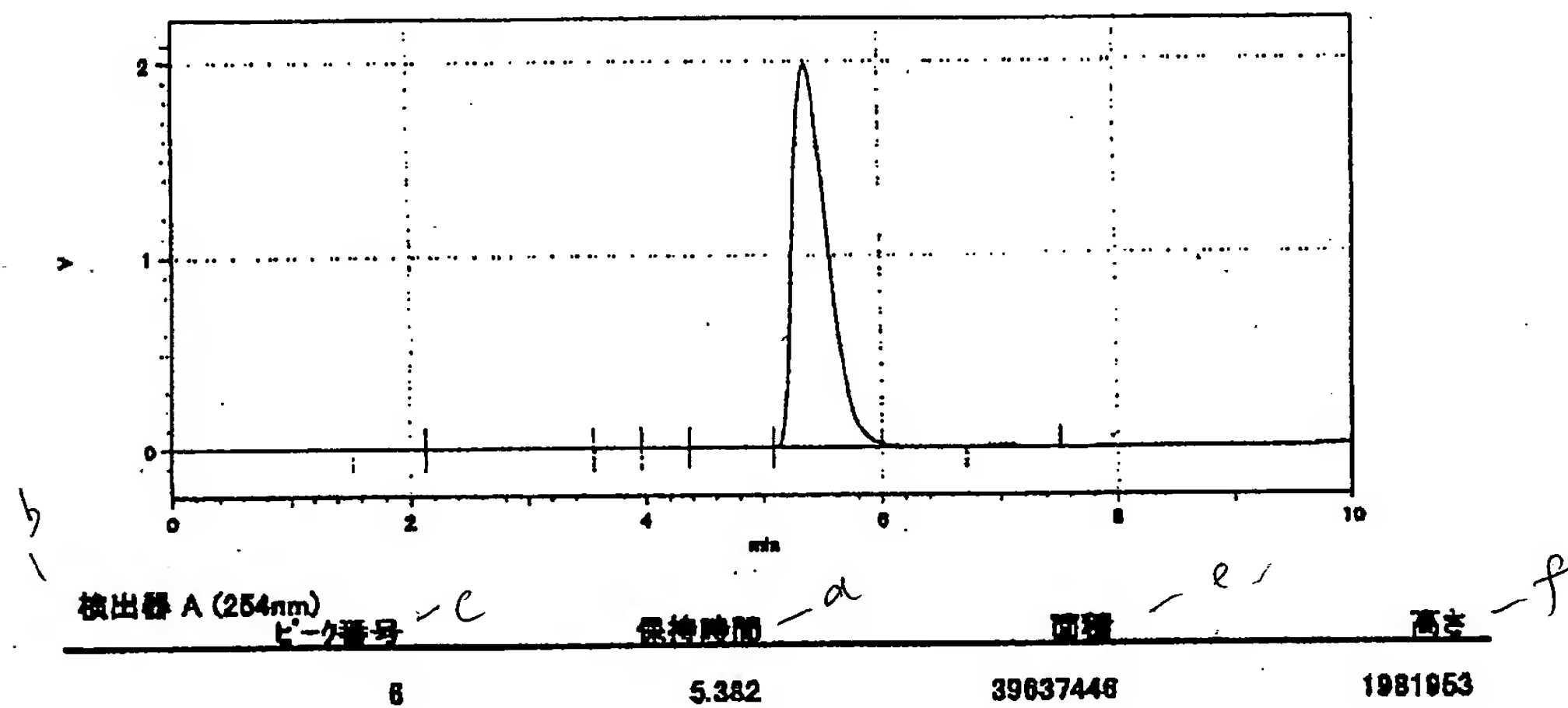
【図1】 Fig. 1



【図2】 Fig. 2

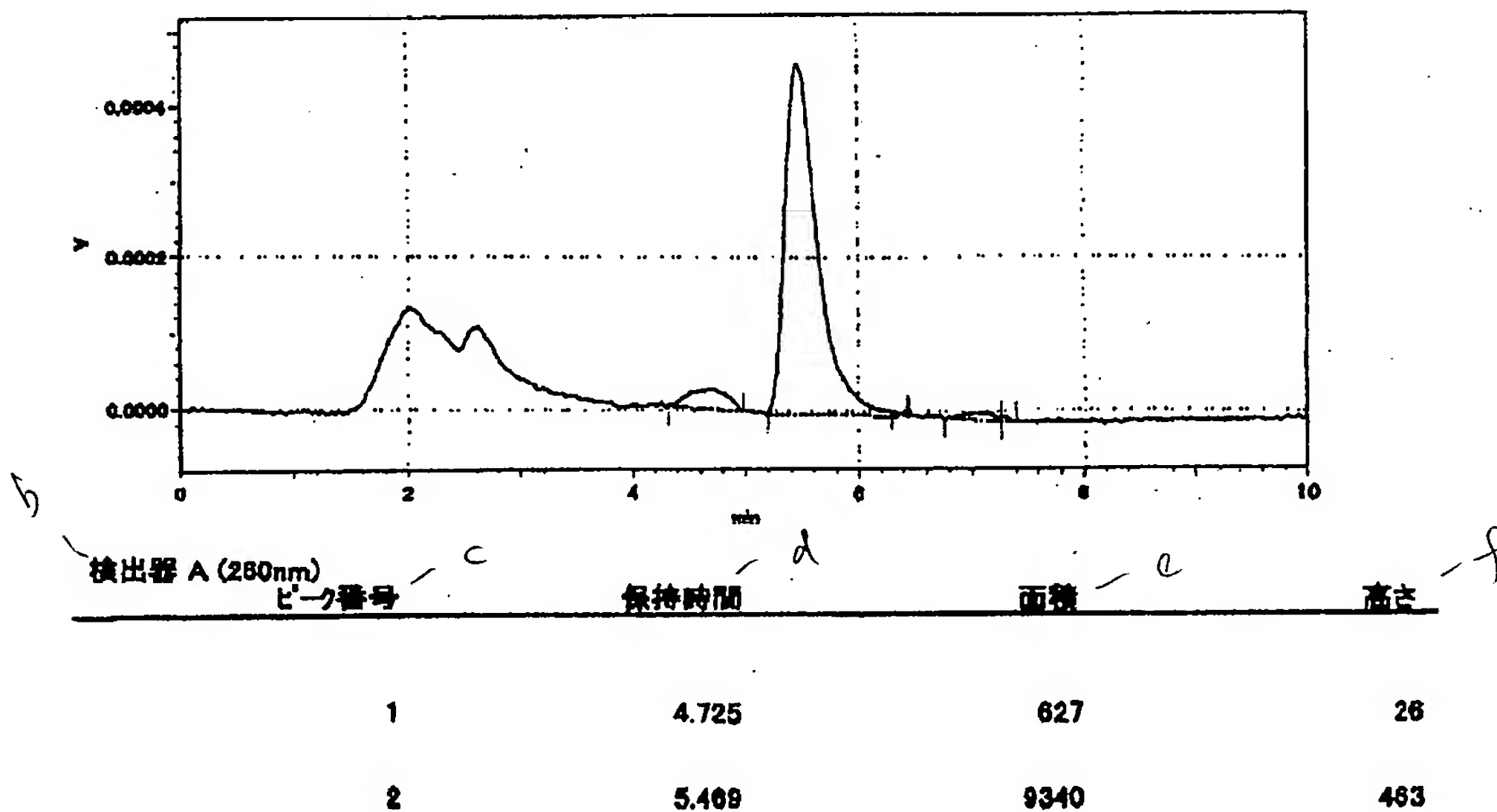
(a)

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(b)

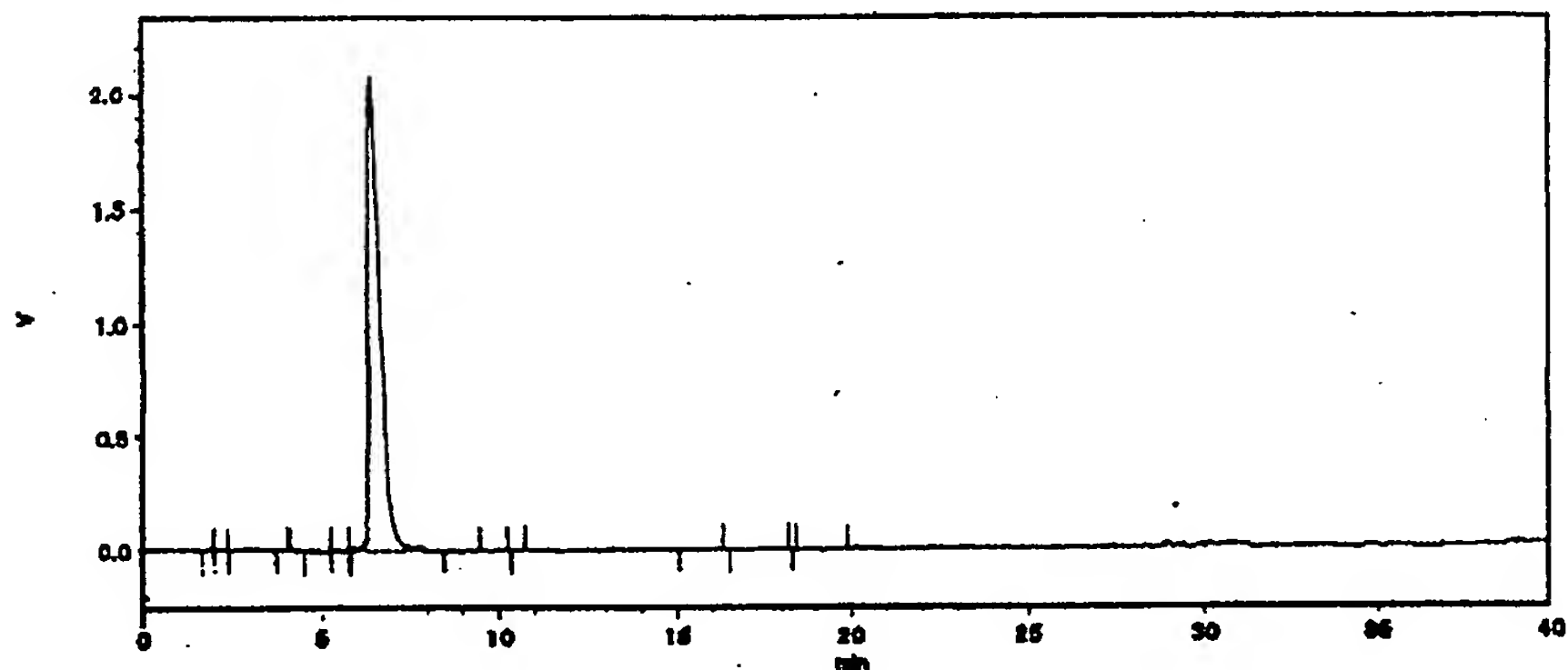
VIAL No. = 70 注入量: 2



【図3】 Fig 3

(a)

VIAL No.= 10 注入量: 2



検出器 B (280nm)

保持時間

6.525

面積

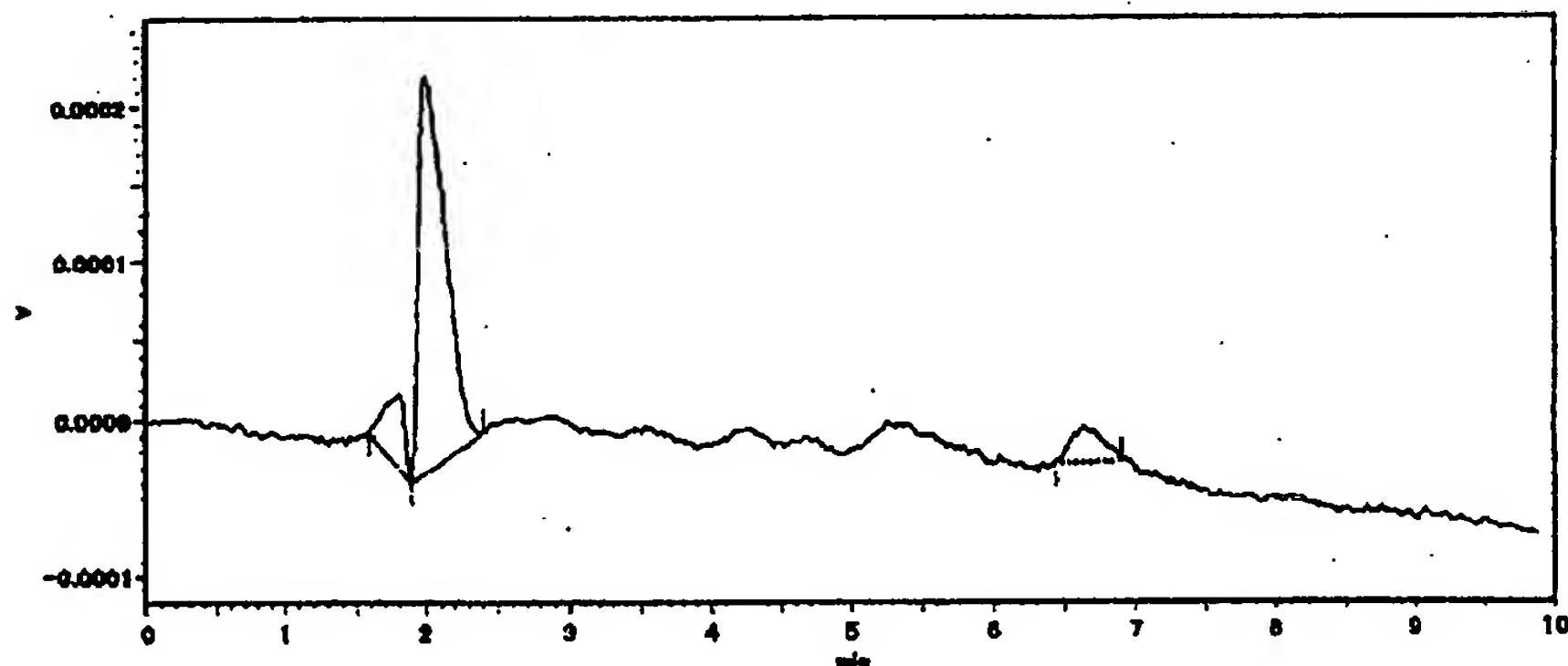
49126367

高さ

2067405

(b)

VIAL No.= 40 注入量: 2



検出器 B (280nm)

保持時間

6.653

面積

321

高さ

22

【図4】 Fig. 4

